REMARKS

The specification has been amended to insert the substitute Sequence Listing submitted herewith.

Claims 29-32, 60, 61, 99-136, 138-146 and 152-166 will be pending upon entry of this amendment. Claims 147-151 have been canceled without prejudice. Claims 29, 30, 60, 61, 99, 105-114, 126-129, 131-136, 138-141 and 146 have been amended for clarity, to remove extraneous language. Claim 101 has been amended to correct a typographical error. Claims 107, 108 and 113 also have been amended to remove recitation of the high stringency hybridization conditions since such recitation is redundant in view of the fact that the hybridization conditions are recited in the base claims from which claims 107, 108 and 113 depend.

New claims 152-166 have been added. New claims 152-163 replace canceled claims 148-151 but claim the same subject matter and are written in independent form. Support for new claims 164 and 165 is found in the specification, *inter alia*, at page 26, lines 17-24 and Figure 8. New claim 166 is supported in the specification, *inter alia*, at page 13, line 33 to page 14, line 19; page 15, lines 4-20; page 78, lines 34-36 and Figure 13.

No new matter is added by these amendments to the specification and claims.

Applicants note that a Revocation and Power of Attorney, executed on behalf of co-assignee Yale University is submitted herewith appointing those listed under Customer Number 20583 as their representatives to prosecute the above-identified application and transact all business at the U.S. Patent and Trademark Office in connection therewith. A Revocation and Power of Attorney executed on behalf of co-assignee Imperial Cancer Research Trust, Ltd. was submitted to the U.S. Patent and Trademark Office on September 9, 2004.

1. **Interview Summary Record**

Applicants' representative, William Thomann, exchanged telephone messages with the Examiner on April 4, 2005 and April 5, 2005 in order to clarify the rejection under 35 U.S.C. § 112, first paragraph, and to determine the status of claims 146-151. In particular, Applicants' representative requested whether the Examiner was referring to SEQ ID NO:26 or SEQ ID NO:24 on page 4 of the Office Action. The Examiner informed Applicants' representative that reference to SEQ ID NO:24 on page 4 of the Office Action was a typographical error and that any citation to SEQ ID NO:24 is actually a citation to SEQ ID NO:26. Further, Applicants' representative requested the status of claims 146-151 which were not accounted for in the Office Action Summary. The Examiner informed Applicants' representative that claims 146-151 are objected to as being dependent on a rejected base claim, but would be allowable if rewritten in independent form.

Applicants and Applicants' representatives thank the Examiner for the clarifications.

2. **Sequence Listing**

In accordance with the Notice to Comply, a copy of which is submitted herewith, Applicants submit paper and computer-readable copies of a substitute Sequence Listing which corrects the deficiencies of the original Sequence Listing, which deficiencies are set forth in the Notice to Comply.

The undersigned hereby states that the content of the paper and computer readable copies of the substitute Sequence Listing, submitted in accordance with 37 C.F.R. §§ 1.821(c) and (e), respectively, are the same. The undersigned further states that the substitute Sequence Listing contains no new matter.

Applicants note that the specification has been amended herein to replace the originally filed Sequence Listing with the substitute Sequence Listing submitted herewith.

Applicants respectfully request that the substitute Sequence Listing be entered into the specification and file history of this application.

3. Rejections under 35 U.S.C. § 112, First Paragraph

Claims 29-32, 60, 61, 101-104, 107, 109, 113-125, 129-136 and 142-145 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that this rejection is directed only to antibodies which bind a vertebrate Delta protein encoded by a nucleic acid that hybridizes under high stringency conditions to the human sequence of SEQ ID NO:14 or 26 since these sequences do not alone or together encode a full-length human Delta protein.

Applicants respectfully disagree with the Examiner and note that in order to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time the specification was filed. The case law has made it clear that written description can be satisfied through disclosure of relevant identifying characteristics, *i.e.*, structure, other physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics, such that the inventor is able to define the claimed compound *so as to distinguish it from other materials.* See, *Amgen, Inc. v. Chugai Pharmaceutical Co., Inc.*, 927 F.2d 1200, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991); *Fiers v. Revel*, 984 F.2d 1164, 25 U.S.P.Q.2d 1601 (Fed. Cir. 1993); *Enzo biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 63 U.S.P.Q.2d 1609 (Fed. Cir. 2002).

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that the conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its methods of preparation, its physical or chemical properties, or whatever characteristics sufficiently

distinguish it.

Amgen, at 1206, 1021 (citations omitted).

> If a conception . . . . requires a precise definition, such as by structure, formula, chemical name, or physical properties, as we have held [in Amgen], then a description also requires that degree of specificity. To paraphrase the Board, one cannot describe what one has not conceived.

Fiers at 1171, 1606.

> The written description requirement can be met by showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Enzo at 960, 1613 (quoting the Guidelines for Examination of Patent Applications under 35 U.S.C. 112 § 1 "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001)). Thus, in order to satisfy the written description requirement, a partial disclosure of the structure can be sufficient, so long as the partial disclosure sufficiently distinguishes the claimed subject matter. There is no requirement under the law that only a full-length, complete structure will satisfy the written description requirement.

Applicants submit that in view of the known functional and structural characteristics of antibodies and routine art-recognized methods of making antibodies, an antibody to a protein meets the written description requirements of Section 112 when the protein to which the antibody binds is described in the claims so as to recite structural characteristics that uniquely identify it and distinguish it from other proteins. See Example 16, pages 59-60 of the Revised Interim Written Description Guidelines Training Materials, available from the U.S. Patent and Trademark Office website (http://www.uspto.gov/web/menu/written.pdf). Applicants submit that the human Delta protein and nucleic acid sequences disclosed in the present specification and recited in the claims are clearly sufficient to distinguish the human Delta protein and its encoding nucleic acids from other proteins and nucleic acids, respectively.

In particular, the specification discloses nucleotide (SEQ ID NOS:14 and 26)

and amino acid (SEQ ID NOS:23 and 65-80) sequences of the partial human Delta clone (Section 8, Figures 10-14). As described on page 76 of the specification, SEQ ID NO:14 is a PCR amplification product of a part of human Delta obtained from a human genomic library, and the encoded amino acid sequence was determined by eye using the full-length chick Delta amino acid sequence as a guide[1].

As discussed on page 78, lines 5-30, Figure 12B shows the nucleotide sequence (now SEQ ID NO:26) of the partial nucleotide contig sequence of human Delta and the amino acid sequences generated by the three predicted reading frames. Amino acid sequence homology to the full-length mouse Delta sequence was determined by eye, and those sequences with the greatest homology were boxed in Figure 12B and represent the predicted amino acid sequence of the human Delta protein. The composite sequence is shown in Figure 14, with the individual sequences composing it assigned SEQ ID NOS:65-80, respectively.

Applicants invite the Examiner's attention to Exhibit A. Exhibit A is a print-out of the full-length human Delta amino acid sequence, which sequence is found in GenBank under Accession No. O00548 (GI#3121982) and which sequence was last updated in the database on July 15, 1998. Exhibit A shows where SEQ ID NOS:65-80 from Figure 14 fall within the full-length human Delta protein in a color-coded fashion. As evidenced by Exhibit A, SEQ ID NOS:65-80 depict approximately 508 out of 723 amino acids (about 70%) of the human Delta protein sequence. Thus, the specification describes nucleic acids that encode more than two thirds of the human Delta protein. This 70% part of the human Delta amino acid sequence and its encoding nucleotides are clearly sufficient to distinguish the

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[1] Applicants note that comparison by eye to the full-length human Delta nucleotide sequence and its encoded protein, presently existing in GenBank under Accession No. AF003522, reveals that SEQ ID NO:14 contains an intron starting at nucleotide 290, and, thus, nucleotides 290 to 412 of SEQ ID NO:14 (erroneously presented as encoding predicted amino acids 99 to 138 of Figure 11) are not coding nucleotides. However, the comparison also reveals that about 110 of the amino acids presented in Figure 11 are identical to the GenBank sequence, and that Figure 11 includes about 28 amino acids carboxy-terminal to SEQ ID NO:80.

human Delta amino acid and nucleotide sequences, respectively, from other amino acid and nucleotide sequences.

Further, Delta proteins have a high degree of structural and functional homology to each other, and the specification also discloses the nucleotide and amino acid sequences of full-length chick Delta and full-length mouse Delta, as well as the amino acid sequences of full-length *Xenopus* and *Drosophila* Delta (see Figures 1A-1B, 2, 3, 4, 7-9). As explained in the specification in Section 5.6.1 on pages 36-37; page 69, lines 13-37; page 7, lines 36 to page 8, line 8; and in Figure 3, Delta proteins are cell-surface expressed proteins that share domain homology (extracellular domain, DSL domain, EGF-like repeat domain, transmembrane domain, intracellular domain), as well as structural conservation, *i.e.*, the order of the domains from N-terminus to C-terminus in the Delta protein.

Applicants respectfully submit that a disclosure of over 500 amino acids amounting to about 70% of the full length human Delta protein (as well as the full length protein sequences of chick Delta, *Drosophila* Delta, *Xenopus* Delta and mouse Delta, which provide additional structural information), is more than sufficient to uniquely identify human Delta and distinguish it from other proteins. Thus, where there is a sufficient written description of the full-length human Delta protein, of which SEQ ID NOS:65-80 are a uniquely identifying part encoded by SEQ ID NO:26, and of which SEQ ID NO:14 encodes a uniquely identifying part, said written description is more than sufficient to convey to the skilled artisan that Applicants described the subject matter at issue, *i.e.*, antibodies to a vertebrate Delta protein, which protein is encoded by a nucleic acid or its complement that hybridizes under high stringency conditions to SEQ ID NO:14 or SEQ ID NO:26.

In view of the foregoing, Applicants respectfully submit that the rejection under 35 U.S.C. § 112, first paragraph, has been overcome. Therefore, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicants respectfully request that the above-made remarks of the present response be entered and made of record in the file history present application.

Applicants request that the Examiner call Adriane M. Antler at (212) 326-3630 if any questions or issues remain.

Respectfully submitted,

Date: May 2, 2005

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Enclosures